# Substitution of smokeless tobacco for cigarettes in Buerger's disease does not prevent limb loss

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**Buerger's Disease, characterized by segmental, inflammatory, occlusive disease of the distal small and medium sized arteries, predominantly affects young men who are cigarette smokers. The disease may lead to ischemia, necrosis, and amputation of distal extremities; most patients have significant improvement in symptoms if smoking is discontinued. We report a patient who experienced progression of biopsy-proven Buerger's disease, after substituting smokeless tobacco for cigarettes. The patient's disease was severe enough to eventually require bilateral below-knee amputations. The association of smokeless tobacco with progressive limb ischemia should lead clinicians to discourage the substitution of smokeless tobacco for cigarette smoking in patients with Buerger's disease. (J Vasc Surg 2008;48:210-2.)**

Buerger's disease is associated with significant morbidity, ranging from ischemic rest pain to extremity amputation. Most patients smoke heavily and experience a dramatic improvement in symptoms and disease progression following smoking cessation.[1,2] This report identifies a patient who experienced significant disease progression after substituting smokeless tobacco for cigarettes. Smokeless tobacco has not been definitively reported to be associated with Buerger's disease, but should be avoided, based on our experience with this patient.

## CASE REPORT

A 21-year-old man with a 6-year history of superficial migratory thrombophlebitis was referred for an ulcer of his left third toe and an infected toenail on his great toe of the same foot. The patient reported he had previously smoked one-half pack of cigarettes daily per year and had recently been advised to discontinue cigarettes, so he substituted smokeless tobacco, eventually consuming as much as one can daily over 5 years. He had no significant exposure to secondhand smoke by history. At the time of referral, he had no other atherosclerotic risk factors.

The patient complained of instep foot claudication, which had progressed to ischemic rest pain bilaterally in both feet. The patient denied any trauma to the skin of the involved digit or extremity. Tests, including a complete blood count, erythrocyte sedimentation rate, platelets, prothrombin time/partial thromboplastin time, factor V Leiden, anticardiolipin antibodies, homocysteine, protein C, and protein S to screen for hypercoagulability, were normal. Rheumatoid factor, antinuclear antibody, and lupus erythematosus cell preparation were also normal. Skin biopsies revealed chronic dermatitis, with moderate perivascular lymphocytic infiltrates and erythema induratum. An erythematous area on the third digit of his left foot became cyanotic, nodular, and eventually ulcerated. The patient was started on cefotaxime and our vascular surgery team was consulted for evaluation and treatment of the ulcer.

On physical examination, upper and lower extremity peripheral pulses were normal to the elbow and knee, respectively. The radial pulse was absent on the right side, and the dorsalis pedis and posterior tibial pulses were absent bilaterally. Ankle-brachial indexes were not obtainable and toe plethysmography waveforms were flat. Both feet demonstrated ischemic changes, with dependent rubor and atrophic, mottled skin. There was a 2-cm gangrenous ulcer on the third digit of the left foot with pus easily expressible. The toenail on the great toe was infected and separated from its bed. Pentoxifylline (Trental) and nifedipine (Procardia) were instituted to improve peripheral blood flow but were ineffective.

Radiographs suggested osteopenia of the second through fifth digits bilaterally with osteomyelitis of the distal left third toe. Digital subtraction arteriography revealed normal aorta, iliac, and femoral arteries. There was occlusion of the peroneal, posterior tibial, and anterior tibial arteries bilaterally with collateralization of the small vessels in the foot (Fig 1), typical for Buerger's disease. The distal vessels were inadequate for bypass. A venogram showed an abnormal superficial venous system with an appearance indicative of prior thrombosis with recanalization.

Angiography of the upper extremities (Fig 2) was performed to evaluate the arterial anatomy after the patient presented later with an ischemic finger. The angiogram of the right hand digits (Fig 2, *A*) and wrist (Fig 2, *B*) demonstrated arterial disease typical of Buerger's disease. No disease was observed in the proximal forearm arteries.

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**Fig 1.** Angiography of left lower extremity prior to below-knee amputation. Left foot angiogram demonstrates typical Buerger's disease findings with occlusion of arteries and "corkscrew" collaterals.

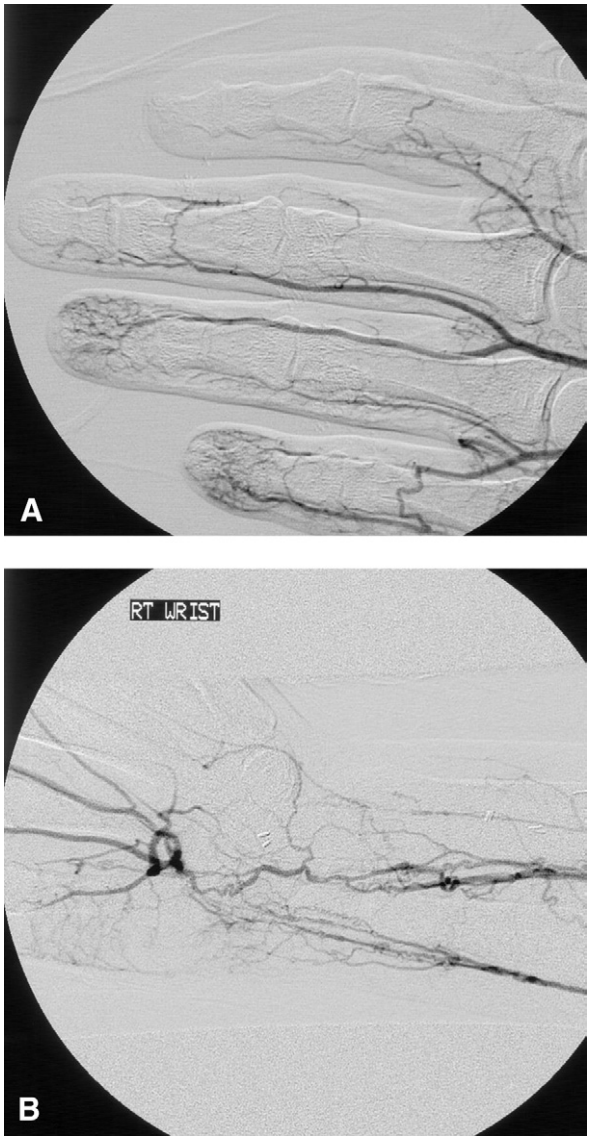


**Fig 2.** Angiography of right upper extremity prior to first below-knee amputation. A, Magnified views of the right hand demonstrate digital artery occlusion. B, Angiogram of the right wrist shows occlusion of the radial and ulnar arteries with normal appearing arteries in the palmar arch. "Corkscrew" collaterals are adjacent to the ulnar artery.

The patient was advised to discontinue use of smokeless tobacco permanently. Thrombolytic therapy and angioplasty re-established flow through the left popliteal artery, but infrapopliteal arteries could not be recanalized. The first and third digits did not improve clinically and toe amputations were eventually performed. The patient was discharged with satisfactory healing of the toe amputations and treated for osteomyelitis with antibiotics.

The patient returned 6 months later (Table) with worsening left foot digital ischemia and required below-knee amputation. It was learned that the patient had continued to use excessive quantities of smokeless tobacco (one can per day) despite our strongest advice to abstain. Although the patient eventually quit chewing tobacco, several revascularization procedures were attempted and failed over the next 3 years. Intraoperative angiograms during femoral-posterior tibial and femoral-peroneal bypasses demonstrated poor outflow vessels and both grafts occluded within 30 days. He eventually required a below-knee amputation of the right leg.

Segmental occlusive thrombi with lymphocytic infiltrates or microabscesses were observed in the amputation specimens. These histological analyses repeatedly confirmed the clinical diagnosis of Buerger's disease. The patient now has bilateral below-knee amputations and walks with two prostheses. He has since discontinued the use of smokeless tobacco and has had no further disease progression in his upper extremities.

## DISCUSSION

Buerger's disease, or thromboangiitis obliterans, once considered a variant of atherosclerosis, is now recognized as a distinct clinical and pathologic entity.[3,4] The characteristic pathologic lesions have a pattern of segmental occlusive thrombi with lymphocytic infiltrates or microabscesses of

**Table.** Timeline of clinical events

| | *Months* |
|---|---|
| Consultation by our vascular team | 0 |
| Thrombolytic therapy and left popliteal angioplasty | 1 |
| First and third toes amputated from left foot | 2 |
| Left leg below-knee amputation | 8 |
| Right leg femoral-posterior tibial bypass – failed | 10 |
| Right leg femoral-peroneal bypass – failed | 11 |
| Right leg below-knee amputation | 13 |

the tunica media in small and medium-sized arteries and veins, which can be observed histologically.[5] The most common clinical presentation is a young male, like our patient, who uses tobacco and complains of foot claudication, pain, or ulcers. Findings include migratory superficial thrombophlebitis, diminished peripheral pulses and symptoms of ischemia, such as rubor, skin atrophy, skin ulceration, cyanosis, and paresthesias in distal extrimeties.[1,2,6] It is important to rule out other disorders, including hypercoagulable profiles, as there is no definitive laboratory test for Buerger's disease; however, histological study of a biopsy sample is helpful in diagnosis.

The observation that continued cigarette smoking exacerbates Buerger's disease while cessation of smoking usually results in dramatic improvement is well established. What has not been emphasized is the relationship between smokeless tobacco and Buerger's disease. Under the pretext of a harm-reduction method, some physicians have advised patients to replace cigarette smoking with smokeless tobacco, if they are unable to discontinue smoking[7,8]; this is the reason why our patient had switched to smokeless tobacco. We report this case to inform clinicians that the same association exists between smokeless tobacco and Buerger's disease as exists between cigarette smoking and Buerger's disease, so that further morbidity can be prevented in these patients.

While one report hypothesizes that the frequency of Buerger's disease will increase with the increase of athletes' use of smokeless tobacco,[9] we are aware of only two other suggestions of a potential relationship between thromboangiitis obliterans and smokeless tobacco.[10,11] In these reports, the patients used smaller quantities of smokeless tobacco (one and one-half cans per week) and were not well documented Buerger's patients. In contrast, our patient used a large quantity of smokeless tobacco (five to seven cans per week), and we have tissue obtained following several amputations to confirm and reconfirm the diagnosis.

Although Buerger's disease may rarely occur in the absence of tobacco use, the overwhelming majority of patients smoke and experience dramatic improvement following cessation.[12,13] Our patient abstained from cigarettes following his Buerger's disease diagnosis and switched to smokeless tobacco, believing it to be an acceptable substitute. Despite aggressive medical treatment and repeated counseling, he continued to use smokeless tobacco and his disease progressed. Only after his initial below-knee amputation did the patient quit; however, the disease at that time was so extensive that his contralateral leg could not be salvaged.

Our report provides strong evidence for the association between smokeless tobacco use and development of Buerger's disease and supports other literature relating tobacco use to vascular disease. Complete abstinence from the use of all tobacco, including cigarettes, cigars, and smokeless tobacco, is advisable in these patients.

## REFERENCES

1. Sasaki S, Sakuma M, Yasuda K. Current status of thromboangiitis obliterans (Buerger's disease) in Japan. Int J Cardiol 2000;75:175-81.
2. Joyce JW. Buerger's Disease (thromboangiitis obliterans). Rheum Dis Clin North Am 1990;16:463-70.
3. McKusick VA, Harris WS, Otteson OE, Goodman RM, Shelley WM, Bloodwell RO. Buerger's Disease: a distinct clinical and pathologic entity. JAMA 1962;181:5-12.
4. Adar R, Papa MZ, Schneiderman J. Thromboangiitis obliterans: an old disease in need of a new look. Int J Cardiol 2000;75:167-70.
5. Kobayashi M, Ito M, Nakagawa A, Nishikimi N, Nimura Y. Immunohistochemical analysis of arterial wall cellular infiltration in Buerger's disease (endarteritis obliterans). J Vasc Surg 1999;29:451-8.
6. Buerger L. Thromboangiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med Sci 1908;136: 567-80.
7. Hatsukami DK, Lemmonds C, Tomar SL. Smokeless tobacco use: harm reduction or induction approach? Prev Med 2004;38:309-17.
8. Gupta R, Gurm H, Bartholomew JR. Smokeless tobacco and cardiovascular risk. Arch Intern Med 2004;164:1845-9.
9. Cohn SL, Taylor WC. Vascular problems of the lower extremity in athletes. Clin Sports Med 1990;9:449-70.
10. O'Dell JR, Linder J, Markin RS, Moore GF. Thromboangiitis obliterans (Buerger's disease) and smokeless tobacco. Arthritis Rheum 1987; 30:1054-6.
11. Lie JT. Thromboangiitis obliterans (Buerger's disease) and smokeless tobacco. Arthritis Rheum 1988;31:813-4.
12. Council on Scientific Affairs. Health applications of smokeless tobacco use. JAMA 1986;255:1038-44.
13. Connoly GN, Winn DM, Hecht SS, Henningfield JE, Walker B, Hoffman D. The reemergence of smokeless tobacco. N Eng J Med 1986; 314:1020-7.

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